REMARKS

I. STATUS OF THE APPLICATION

Claims 1 – 26 were filed in the original application. In response to the Restriction Requirement in the Office Action mailed April 10, 2006, the Applicants cancelled claims 1 – 26, 30, and 39 – 49, and added claims 50 – 87. In a previous Response to the Office Action of July 27, 2006 the Applicants cancelled claims 36, 61, 72 and 79, and amended claims 27, 28, 37, 53, 62, 69, 73, 75, and 80. In the present Amendment and Response to Final Office Action of May 11, 2007 the Applicants have amended claims 27, 53, 69 and 75. Therefore, claims 27-29, 31-35, 37, 38, 50-60, 62-71, 73-78, 80-87 are currently pending.

The Applicants submit that the present amendments to the claims add no new subject matter. With regard to independent claims 17, 53, 69, support for the amendment "contacting nucleic acid from said pathogen with a plurality of different primer pairs wherein at least one primer pair of said plurality of primer pairs hybridizes to flanking sequences of said nucleic acid, wherein said flanking sequences flank at least one variable nucleic acid sequence", and for independent claim 75 "contacting nucleic acid from said one or more etiologic agents of disease with a plurality of different primer pairs wherein at least one primer pair of said plurality of primer pairs hybridizes to flanking sequences of said nucleic acid, wherein said flanking sequences flank at least one variable nucleic acid sequence of said etiologic agent of disease" may be found throughout the Specification at, for example, page 18, lines 6-15:

> "In some embodiments, broad range survey intelligent primers are capable of identification of bioagents at the species level. One main advantage of the detection methods of the present invention is that the broad range survey intelligent primers need not be specific for a particular bacterial species, or even

genus, such as Bacillus or Streptomyces. Instead, the primers recognize highly conserved regions across hundreds of bacterial species including, but not limited to, the species described herein. Thus, the same broad range survey intelligent primer pair can be used to identify any desired bacterium because it will bind to the conserved regions that flank a variable region specific to a single species, or common to several bacterial species, allowing unbiased nucleic acid amplification of the intervening sequence and determination of its molecular weight and base composition."

And page 65, lines 5-9:

"In accordance with the present invention an approach of broad PCR priming across several different viral species is employed using conserved regions in the various viral genomes, amplifying a small, yet highly informative region in these organisms, and then analyzing the resultant amplicons with mass spectrometry and data analysis."

With regard to independent claims 27 and 69, support for "comparing said base composition of said amplification product to calculated or measured base compositions of analogous amplification products of one or more known pathogens present in a database comprising 5 or more base compositions.", and support for "comparing said base composition of said amplification product to calculated or measured base compositions of analogous amplification products of one or more known etiologic agents of disease present in a database comprising 5 or more base compositions" of independent claim 75, may be found throughout the Specification at, for example, page 13, lines 11-13 :

"FIG. 27 shows a representative base composition distribution of *poxviruses* for a single primer pair region on the DNA-dependent polymerase B gene (DdDpB). The spheres represent different *poxvirus* sequences that were used for primer design."

And page 64, lines 11-13:

"As illustrated in FIG. 27, members of the *Orthopoxvirus* genus group can be identified, distinguished from one another, and distinguished from other members of the Poxvirus family using a single pair of primers designed against the DdRpB gene."

And page 64, line 14 – page 65, line 2:

"Since the primers were designed across regions of high conservation within this genus, the likelihood of missed detection due to sequence variations at these sites is minimized. Further, none of the primers is expected to amplify other viruses or any other DNA, based on the data available in GenBank. This method can be used for all families of viral threat agents and is not limited to members of the *Orthopoxvirus* genus."

Accordingly, Figure 27. provides express support for a database comprising a plurality of base compositions corresponding to 5 or more pathogens, for example, Variola virus, Monkeypox virus, Camelpox virus, Cowpox virus and Vaccinia virus.

With regard to independent claim 53, support for "comparing said base composition of said amplification product to calculated or measured base compositions of analogous amplification products of one or more known strain types of said pathogen present in a database comprising 4 or more base compositions." may be found throughout the Specification at, for example, at page 12, lines 6-10

"FIG. 21 shows a representative base composition distribution of human adenovirus strain types for a single primer pair region on the hexon gene. The circles represent different adenovirus sequences in our database that were used for primer design. Measurement of masses and base counts for each of the unknown

samples A, B, C and D matched one or more of the known groups of adenoviruses."

And page 55, line 22 – page 57, line 3:

"All available genomic sequences for human adenoviruses available in public databases were surveyed. The hexon gene was identified as a candidate likely to have broad specificity across all serotypes. Four primer pairs were selected from a group of primers designed to yield broad coverage across the majority of the adenoviral strain types (Table 9) wherein Tp=5'propynylated uridine and Cp=5'propynylated cytidine.

"These primers also served to clearly distinguish those strains responsible for most disease (types 3, 4, 7 and 21) from all others. DNA isolated from field samples known to contain adenoviruses were tested using the hexon gene PCR primers, which provided unambiguous strain identification for all samples. A single sample was found to contain a mixture of two viral DNAs belonging to strains 7 and 21.

"Test results (FIG. 21) showed perfect concordance between predicted and observed base composition signatures for each of these samples. Classical serotyping results confirmed each of these observations."

Accordingly, Figure 21. provides express support for a database comprising a plurality of base compositions corresponding to 4 or more strain types, for example, adenovirus strain types 3, 4,7 and 21.

The Applicants note that all amendments and cancellations of claims are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG),[1] and without waiving the right to prosecute the amended or cancelled claims (or similar claims) in the future.

1 65 Fed. Reg. 54603 (Sept. 8, 2000).

In the Final Office Action of May 11, 2007 there are 2 rejections. The currently pending rejections are:

1. Claims 27, 28, 32-34, 36-38, 50, 69, 70, 73-76, 80, 81, 84 and 85 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Hurst *et al.* (Rapid Comm. Mass Spectrom. (1996) 10:377-382.), (hereinafter "Hurst") in view of either Muddiman *et al*. (Anal. Chem. (1997) 69:1543-1549) (hereinafter "Muddiman") or Chen (U.S. Patent 6,613,509) (hereinafter "Chen").

2. Claims 27-29, 31-35, 37, 38, 50-60, 62-71, 73-78 and 80-87 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable Hoffman *et al.* (Arch. Virol. (2001) 146:2275-2289.) (hereinafter "Hoffman") in view of Koster (WO 98/20166) (hereinafter "Koster") and further in view of Muddiman or Chen.

II. Rejections Under 35 U.S.C. 103(a)

A *prima facie* case of obviousness requires the Examiner to cite to a reference which a) discloses all the elements of the claimed invention, b) suggests or motivates one of ordinary skill in the art to combine the claim elements to yield the claimed invention, and c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements negates a finding of a *prima facie* case and, without more, entitles the Applicants to allowance of the claims in issue. (MPEP)

In the Final Office Action of May 11, 2007, the Examiner notes with reference to the Declaration of Dr. Stephan Buchsbaum incorporated in the Amendment and Response to Final Office Action of December 20, 2006:

"As noted in the response to the Declaration, the unexpected nature of the results was based upon the "broad range priming" and the database of agents. Neither of these elements is present in the current claims and therefore, neither of these elements can be relied upon to overcome the prior art." (Final Office Action of May 11, 2007, page 18).

And:

"The declaration points to the combination of these two elements as provided the unexpected result, which is not present in the current claim set. Therefore, the argument of skepticism of experts is not persuasive since the skepticism is not directed towards the actual claims of the current application, but rather to a narrower claim set, not currently present." (Final Office Action of May 11, 2007, page s 18 – 19).

Accordingly, without acquiescing to any of the Examiner's arguments or rejections, and without waiving the right to prosecute the amended claims (or similar claims) in the future, in the present Amendment and Response to Final Office Action of May 11, 2007 the Applicants have amended independent claims 27, 53, 59 and 75. For example, independent claim 27 is amended to read "a plurality of different primer pairs wherein at least one primer pair of said plurality of primer pairs hybridizes to flanking sequences of said nucleic acid, wherein said flanking sequences flank at least one variable nucleic acid sequence", and "comparing said base composition of said amplification product to calculated or measured base compositions of analogous amplification products of one or more known pathogens present in a database comprising 5 or more base compositions."

The Applicants submit that there is no motivation to combine the cited references in the manner suggested by the Final Office Action of May 11, 2007, and, even if combined, there would be no expectation of success. To advance prosecution of the

present application, in the Amendment and Response to Final Office Action of December 20, 2006 the Applicants have presented a Declaration under 35 C.F.R. §1.132 by Dr. Steven Buchsbaum, a former Program Manager for the Defense Advanced Research Projects Agency (DARPA). In the Declaration, Dr. Buchsbaum notes the unexpected success of the methods described in the claims (see paragraph 3), the successful funding of a long-felt need (see paragraph 4), as well as provides independent commentaries and high visibility publications regarding the claimed technology (see paragraphs 5-10 and corresponding exhibits).

In view of the amendments to the claims and the accompanying Declaration, the Applicants respectfully submit that the claims are in condition for allowance.

III. DOUBLE PATENTING

Claims 27-29, 31-35, 37, 38, 50-60, 62-71, 73-78 and 80-87 are rejected under the doctrine of obviousness-type double patenting as allegedly being un-patentable over claims 1-29 of U.S. Patent No. 7,108,974. In the same paragraph of the same rejection (*i.e.*, "5." of the Final Office Action of May 11, 2007 pages 12 –13, the Examiner notes:

> "Therefore, the species of claims 59, 60, 62, 63, 66, 69-76 and 79-94 of co-pending Application No. 10/156,608 anticipates the current more generic claims and renders them prima facie obvious."

The Applicants submit that it is not clear which reference provides the basis for the Examiner's rejection (*i.e.*, U.S. Patent No. 7,108,974, copending Application No. 10/156,608, or both). In turn, upon indication of otherwise allowable subject matter, the Applicants will consider the filing of a Terminal Disclaimer.

Claims 27-29, 31-35, 37, 38, 50-60, 62-71, 73-78 and 80-87 are provisionally rejected under the doctrine of obviousness-type double patenting as allegedly being unpatentable over particular claims of numerous co-pending applications *i.e.*, 10/660,997,

10/660,996, and 10/660,122. Upon indication of otherwise allowable subject matter, the Applicants will consider the filing of a Terminal Disclaimer.

CONCLUSION

All grounds of rejection of the Final Office Action of December May 11, 2007 have been addressed, and reconsideration of the application is respectfully requested. It is respectfully submitted that Applicant's claims as amended should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (608) 218-6900.

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